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# Binaural interaction and the effects of stimulus intensity and repetition rate in human auditory brain-stem

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**Abstract**

Binaural interaction (BI) components in brain-stem auditory evoked potential (BAEP) and their changes with stimulus intensity and repetition rate were examined in human adult. Seven BI components were identified, which occurred between the latency range of 5 and 11 ms and coincided consistently with the latency range of BAEP waves IV–VII. Waves DV and DVII, occurring at the downslopes of BAEP waves V and VII, respectively, were the two most prominent and reproducible BI components. Wave DVII existed consistently at high, moderate and, in most cases, low stimulus intensities, suggesting that this component is neurogenic although acoustic cross-talk may account for a part of its waveform at high stimulus intensities. The latencies of all BI components increased as a function of decreasing stimulus intensity, while the interpeak intervals, especially DV–DVII, were essentially constant at different intensity levels. The amplitudes of BI components decreased slightly with decreasing intensity. As click repetition rate increased, BI wave latencies and interpeak intervals increased slightly and amplitudes decreased slightly. When repetition rate increased to above 20/s, BI components became poorly differentiated. Lower repetition rates, e.g. 10/s, are therefore preferred for routine derivation of the BI. The changes in the latency and amplitude of BI components with stimulus intensity and repetition rate were associated or concomitant with those of the corresponding BAEP components in monaural and binaural potentials. In view of the concomitant relationship between BI and BAEP latency, we designate BI components in association with the corresponding BAEP components.

*Keywords:* Binaural interaction; Binaural hearing; Audition; Brain-stem auditory evoked potentials

## 1. Introduction

In the central auditory pathway, at least 80% of the neurons are influenced by stimulation of either ear (Irvine, 1986; Moore, 1991). Binaural interaction (BI) reflects electrophysiological activity of these binaurally influenced neurons central to the cochlear nucleus, and is the substrate for psychoacoustic function of sound localization and lateralization. This phenomenon has been observed to be prominent in the extracellular activity recorded from brain-stem auditory units, and occurs at most levels of the brain-stem auditory pathway. BI in the auditory brain-stem occurs primarily and almost simultaneously at 3 levels of the brain-stem: the superior olivary complex, the nuclei of lateral lemniscus and the inferior colliculus (Moore, 1991). In auditory evoked potentials, BI, a derived neural interaction, is defined as any difference between the potentials to binaural stimulation and the summed monaural potentials (Dobie and Berlin, 1979). Measurement of BI is usually patterned after the technique of Kemp and Robinson (1973) and Wernick and Starr (1968). Potentials evoked by binaural stimuli should be equal to the sum of the potentials to the right and left stimuli presented monaurally if there is no interaction from the binaural stimulus condition. Any difference between the potentials recorded for binaural stimulus condition and the summed monaural potentials is due to the effect of BI.

Since Jewett first identified BI in brain-stem auditory evoked potential (BAEP) in 1970, the BI has been successfully demonstrated in humans (Hosford et al., 1979; Ain-

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slie and Boston, 1980; Dobie and Norton, 1980; Hosford-Dunn et al., 1981; Levine, 1981; Robinson and Rudge, 1981; Wrege and Starr, 1981; Galbraith et al., 1983; Kelly-Ballweber and Dobie, 1984; Fullerton et al., 1987; Ito et al., 1988; Fowler, 1989; McPherson et al., 1989; Curio and Weigel, 1990; Jones and Van der Poel, 1990; Levine and Davis, 1991; McPherson and Starr, 1993; Polyakov and Pratt, 1994; Jiang and Tierney, 1996b; Jiang et al., 1996) as well as animals such as the guinea pig, dog, cat and ferret. The BI waveform in the BAEP is composed of several components. Previous studies have shown that BI components in the human BAEP occur between the latency range of BAEP wave V to wave VI (Ainslie and Boston, 1980; Levine, 1981; Robinson and Rudge, 1981; Wrege and Starr, 1981; Kelly-Ballweber and Dobie, 1984). So far, interpeak intervals of BI components have not been described. In a pilot study of human BI, we observed that BI waveform appeared beyond the latency range of wave V to wave VI, and the time between various BI components, or the interpeak intervals, were essentially constant.

The BAEP is known to be significantly affected by stimulus intensity and repetition rate. These effects vary with neurophysiological and developmental characteristics of the subject (Thornton and Coleman, 1975; Pratt and Sohmer, 1976; Don et al., 1977; Scott and Harkins, 1978; Pratt et al., 1981; Gerling and Finitzo-Hieber, 1983; Jiang, 1991; Jiang et al., 1991a; Jiang et al., 1991b; Liu and Jiang, 1991; Jiang, 1995). Abnormalities in these effects may be associated with neuropathology in the auditory pathway (Pratt et al., 1981; Gerling and Finitzo-Hieber, 1983; Jiang et al., 1991a; Jiang et al., 1991b; Jiang, 1995). Therefore, understanding of these effects can facilitate assessment of neurophysiology of the auditory pathway, which in turn could help to diagnose neuropathology in diseased conditions. Knowledge of whether BI is affected by stimulus intensity and repetition rate in normal subjects is important for the understanding of physiological properties of neural elements in the brain subserving binaural processing and potentially for the use of BI in diagnosing neuropathology. To date, there is a lack of systematic studies of the effects of stimulus intensity and repetition rate on BI components in the BAEP, although the BI has been observed at different stimulus intensities by several authors. Little is known about whether the possible changes in BI with stimulus intensity and repetition rate occur in concomitance with those of the BAEP. Since more than 80% of the central auditory neurons are influenced by stimulation of either ears and BI is derived from monaurally and binaurally recorded potentials, it is possible that stimulus intensity and repetition rate may exert similar effects on BI and the BAEP.

In order to further characterize BI in human BAEP, the present study examined the effects of stimulus intensity and repetition rate on BI components in human adult BAEP. Special attention was paid to the BI components that occur beyond the latency range previously reported in the literature. Furthermore, the nomenclature used by previous investigators to designate BI components is largely arbitrary and differs greatly. This makes comparison of the results from different investigators inconvenient. Thus, in this reports we introduce a more logical nomenclature for BI components.

## 2. Methods

Recording of the BAEP was carried out in an electrically shielded, darkened and soundproofed room. Seventeen adults aged 18–45 years (9 males and 8 females) participated in the study. They were either staff or medical students at the Departments of Physiology and Perinatal Medicine, University of Sydney. None of the subjects had known hearing or neurological disorders. The requirements for the study were that monaural potential threshold was better than 20 dB normal hearing level (dB nHL, referenced to the average threshold in normal adults) and the threshold difference between the left and right ears was less than 5 dB. Subjects, lying supine on a soft bed, were instructed to be as relaxed as possible. Most slept shortly after the start of the recording.

Auditory evoked potentials were recorded using a commercially available Amplaid Mk 4 system. Three silver cup electrodes were filled with electrode paste, placed along the midline of the scalp at the vertex (Cz, positive), the nape of the neck (negative), and the upper forehead (Fpz, ground), respectively. Interelectrode impedances were maintained below 5 kΩ. Acoustic stimuli were alternating clicks that were generated by delivering 0.1 ms square pulses from a stimulator through an attenuator to a pair of matched TDH-39 earphones encased in cushions. Clicks were presented at the intensity of 70 dB nHL and the repetition rate of 10/s in all cases. Eleven subjects were tested at various click intensities, and 7 were tested at several click repetition rates. The click intensity was decreased from 70 to 10 dB nHL with a separation of 10 or 20 dB. All subjects were tested at 70, 50, 30 and 10 dB nHL. The repetition rate was increased from 10 to 60/s in 10 or 20/s steps. Preamplifier filter settings were 100-2000 Hz. For each recording, the potentials to 2048 stimulus repetitions were averaged. Auditory evoked potentials to monaural and binaural stimulation were recorded separately. The first session of recording was made in the sequence of left monaural, right monaural and binaural stimulation. The second session was simply a replication of the recording but in reverse sequence. Duplicate recordings were made.

There are two contrary procedures to derive BI waveform. One is by subtracting the binaurally evoked potentials from the sum of the monaurally evoked potentials; i.e. BI = (left monaural + right monaural) − binaural or, in short, (L + R) − B (e.g. Hosford-Dunn et al., 1981; Levine, 1981; Wrege and Starr, 1981; Jones and Van der

Poel, 1990). This procedure produces an upward deflection of the BI waveform when the summed monaurally evoked potential is larger than the binaurally evoked potential (L + R > B). The converse is true for a downward deflection (L + R < B). The other procedure, which is just contrary to the above, is by subtracting the sum of the monaurally evoked potentials from the binaurally evoked potentials; i.e. BI = B − (L + R) (e.g. Ainslie and Boston, 1980; Dobie and Norton, 1980; Kelly-Ballweber and Dobie, 1984; Ito et al., 1988; McPherson et al., 1989). Thus, polarity is reversed. In this study, BI trace was obtained by the former procedure, i.e. BI = (L + R) − B. Amplitude was measured 'peak to following trough' for upward waves and 'trough to following peak' for downward waves, i.e. peak-to-peak. Latency was measured from stimulus onset to the peak of a wave. Interpeak interval represented the time between the peaks or troughs of any two BI components.

Means, standard deviations and coefficients of variation (CV) for latency, interpeak interval and amplitude were obtained for all BI components. Five subjects were retested 1.5 months after the initial test to examine intra-individual variation.

## 3. Results

### *3.1. Waveform and nomenclature of BI components*

The derived BI in the BAEP were found to be composed of 3 upward and 4 downward components which occurred between the latency range of 5 and 11 ms. In some BI traces, there were additionally one or two small components, with a latency range corresponding to waves III–IV in BAEP trace and preceding the first BI component. They were variable and less reproducible compared to the above 7 BI components. Fig. 1 illustrates the time domain of BI components in association with that of BAEP waves at high-, moderate- and low-stimulus intensity levels.

BI components were designated with a prefix 'D', referring to the difference between the sum of the monaural potentials and the binaural potentials, followed by the Roman numeral, based on Jewett nomenclature for BAEP waves with which the BI latencies were associated. Thus, 3 upward components were designated as waves DV, DVI and DVII in sequence because they always occurred in association or concomitance with waves V, VI and VII in the BAEP trace, respectively. Accordingly, the subsequent downward components were named as waves DV′, DVI′ and DVII′, respectively, and the first downward component was named as DIV′. The time between various BI components, especially waves DV, DVI and DVII, were fairly constant. Thus, three interpeak intervals of the BI, i.e. DV–DVII, DV–DVI and DVI–DVII, were developed here. The nomenclature of BI components and the methods of measuring amplitude, latency and interpeak interval are shown in Fig. 2. Tables 1 and 2 list means, standard deviations, ranges and CV for wave latencies, interpeak intervals and amplitudes of the BI components.

Waves DV and DVII were the two most prominent,

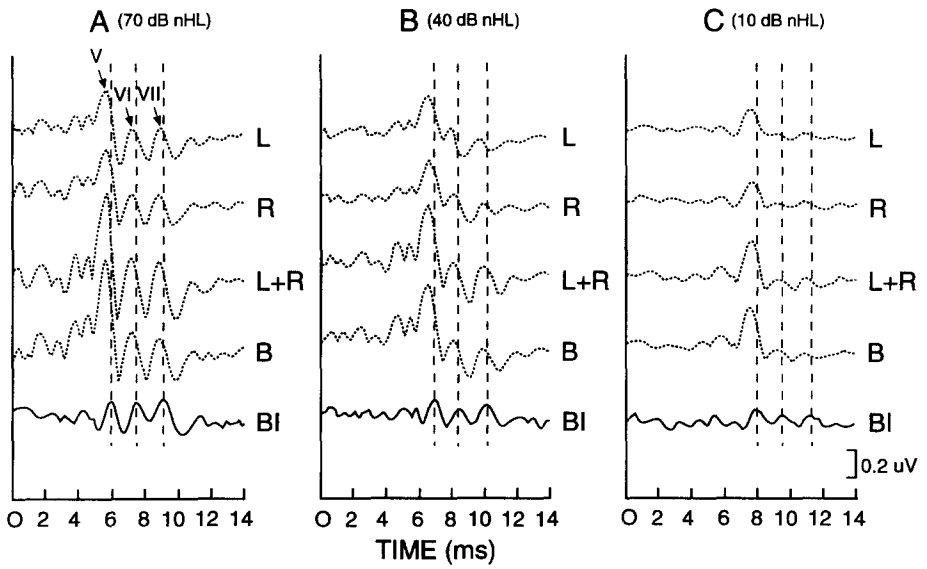


Fig. 1. Composite left (L) and right (R) monaural, summed monaural (L + R), binaural (B), and binaural interaction (BI) waveforms in a subject to demonstrate the time domain of BI components relative to that of corresponding BAEP waves at high (A), moderate (B) and low (C) click intensity levels. The BI trace is derived by subtracting the binaurally evoked potentials from the sum of the monaurally evoked potentials; i.e. BI = (L + R) − B. The stimuli are 0.1 ms clicks at 10/s. Note that 3 upward BI components occur at the latency ranges corresponding to the latencies of the downslopes of waves V, VI and VII, respectively; these corresponding relationships are constant at high-, moderate- and low-intensity; the first and last upward waves are the two most prominent and consistent BI components; at low intensity, most BI components become blurred; BAEP wave VII is significantly larger in the summed monaurally evoked potentials than in the binaurally evoked potential at high click intensity, resulting in a prominent last upward BI component (DVII).

Table 1

Means and standard deviations for latencies and amplitudes of BI components at 70 dB nHL and 10/s clicks

| | DIV′ | DV | DV′ | DVI | DVI′ | DVII | DVII′ |
|---|---|---|---|---|---|---|---|
| *Latency* | | | | | | | |
| Mean (ms) | 5.38 | 6.17 | 6.96 | 7.86 | 8.63 | 9.63 | 10.93 |
| SD (ms) | 0.08 | 0.08 | 0.12 | 0.16 | 0.33 | 0.27 | 0.30 |
| Min (ms) | 4.62 | 5.60 | 6.40 | 7.24 | 7.70 | 8.92 | 10.00 |
| Max (ms) | 5.96 | 6.84 | 7.68 | 8.90 | 9.80 | 10.62 | 12.16 |
| CV (%) | 5.25 | 4.69 | 5.04 | 5.04 | 6.67 | 5.35 | 5.06 |
| *Amplitude* | | | | | | | |
| Mean (μV) | 0.17 | 0.20 | 0.16 | 0.12 | 0.21 | 0.35 | 0.05 |
| SD (μV) | 0.08 | 0.12 | 0.10 | 0.07 | 0.11 | 0.11 | 0.04 |
| Min (μV) | 0.03 | 0.04 | 0.02 | 0.02 | 0.05 | 0.13 | 0.01 |
| Max (μV) | 0.35 | 0.46 | 0.39 | 0.37 | 0.48 | 0.55 | 0.12 |
| CV (%) | 44.97 | 60.97 | 62.65 | 60.21 | 49.72 | 32.56 | 84.30 |

SD, standard deviation; MIN, sample minimum; MAX, sample maximum; CV, coefficient of variation.

consistent and reproducible BI components at high-intensity stimulation. The first downward component was wave DIV′. Its latency was around 5.4 ms and coincident with the latency range of BAEP wave IV to wave V. This component tended to be more evident at moderate stimulus intensity levels than at high or low intensity levels. Wave DV, with a latency of 6.2 ms, always occurred in the region of the descending slope of BAEP wave V and was closer to the negative trough following wave V. The latency of wave DV′ was intermediate between the latencies of the negative trough following wave V and the ascending slope of wave VI in BAEP trace. Wave DVI occurred in the downslope of BAEP wave VI. Its latency was around 7.9 ms. Wave DVI′ appeared in the time domain of the negative trough following wave VI to the ascending slope of wave VII in BAEP trace. This BI component was variable.

The last two upward and downward components in the BI were waves DVII and DVII′. Wave DVII, with a latency range of 8.9–10.6 ms, appeared in the region of the downslope of BAEP wave VII. At high intensity levels of stimulation, wave VII in the summed monaurally evoked potentials was much larger than that in the binaurally evoked potential, producing a large BI component DVII (Fig. 1). Wave DVII usually was the most prominent BI component at high stimulus intensity levels, and existed consistently at moderate and, in some case, low intensity levels. Wave DVII′ occurred shortly after the negative trough following BAEP wave VII, and its waveform was variable.

The above latency association of BI components with the corresponding BAEP waves was constant and independent of click intensity level and repetition rate.

### 3.2. Variation and reproducibility of BI

#### 3.2.1. Inter-individual variation

As shown by CV in Tables 1 and 2, the variation for BI wave amplitudes was appreciable compared to that for wave latencies and interpeak intervals. Of the BI components, waves DV and DVII had the smallest variation and waves DVI′ and DVII′ had the largest. In some cases the waveform of DVII′ was too variable to accurately determine its amplitude value. For interpeak intervals, DV–DVII was fairly constant, whereas DV–DVI and DVI–DVII were relatively variable. Fig. 3 shows BI traces recorded from 6 adults. It can be seen that waves DVII and DV were the two most prominent and consistent BI components.

#### 3.2.2. Intra-individual variation

All BI components, in particular waves DV and DVII, were generally reproducible within a recording session and from session to session. Fig. 4 shows 6 superimposed BI traces recorded consecutively from a subject within 1.5 h. The 4 duplicate traces shown in Fig. 5 are recorded serially from a subject during 5 months with an interval of about every 1.5 months. Waves DV and DVII were more stable and reproducible than the other BI components. Five subjects were tested twice with an interval around 1.5 months. Student's *t* test for comparisons between the BI data from the first and second times did not reveal any significant differences in wave latencies and intervals of the four

Table 2

Means and standard deviations for interpeak intervals (ms) of BI at 70 dB nHL and 10/s clicks

| | DV–DVI | DVI–DVII | DV–DVII |
|---|---|---|---|
| Mean | 1.69 | 1.79 | 3.46 |
| SD | 0.28 | 0.39 | 0.48 |
| Min | 1.12 | 1.26 | 2.90 |
| Max | 2.38 | 2.74 | 4.36 |
| CV (%) | 16.73 | 21.80 | 13.95 |

Abbreviations as in Table 1.

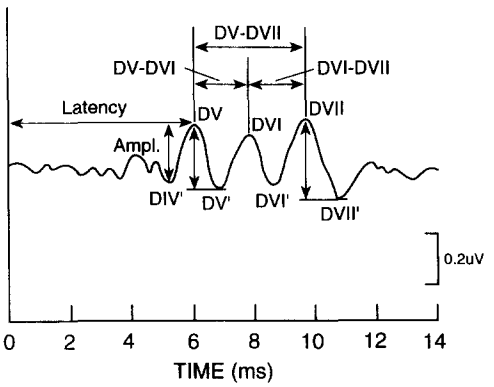


Fig. 2. Schematic drawing indicating the nomenclature of BI components and the measurements of amplitude, latency and interpeak interval. The BI is derived by subtracting the binaurally evoked potentials from the sum of the monaurally evoked potentials.

major BI components, i.e., waves DIV′, DV, DVI and DVII (all $P > 0.05$).

Muscle contaminations had a substantial influence upon BI waveform. It was difficult to obtain reliable and reproducible BI waveform from a nervous or restless subject. On the contrary, well differentiated BI components could be obtained from a subject whose muscles were thoroughly relaxed while recording.

In two very thin female subjects with small head circumference relative to the other subjects, BAEP wave amplitudes in both monaural and binaural potentials were much larger than those in the others. This may be largely due to the relatively shorter geometrical distance between the recording sites and the neural generators in the two females. The amplitudes of BI components were also relatively larger compared to those in the others.

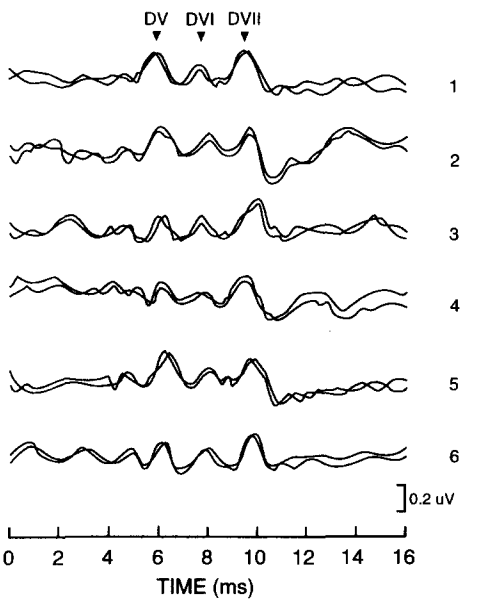


Fig. 3. BI traces derived at 70 dB nHL and 10/s clicks from 6 normal adults, respectively. Duplicate traces in each subject are superimposed for replication. Note that waves DV and DVII are the two most consistent components in the BI waveform and DVII is the most prominent component.

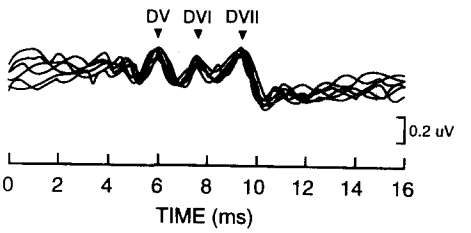


Fig. 4. Six superimposed BI traces showing intra-individual variation of the BI, recorded at 70 dB nHL and 10/s clicks consecutively from a subject within 1.5 h. Among the BI components, waves DV and DVII are most reliable and reproducible.

### 3.3. Effects of stimulus intensity on BI components

In general, a decrease in click intensity decreased the amplitudes of later BI components, in particular wave DVII, more than the earlier ones. Fig. 6 illustrates typical BI waveform at different click intensity levels from a female subject. At high and moderate click intensity levels, most BI components, especially waves DV and DVII, could be clearly differentiated. At low click intensities, only wave DV and, sometimes, wave DVII remained reliably identifiable. Wave DV was the last BI component to disappear. As the click intensity decreased, all BI wave latencies increased and the amplitudes decreased. The change in wave DV amplitude with varying click intensity level was relatively less significant compared to that in BAEP wave V. At 70 dB nHL, wave DV amplitude was equal to 24% (16–28%) of the amplitude of BAEP wave V in the summed monaural potentials (L + R). As the intensity decreased, this percentage increased slightly up to 22–38% at 10 dB nHL.

Figs. 7 and 8 present graphically the mean values of latencies and interpeak intervals of BI components at var-

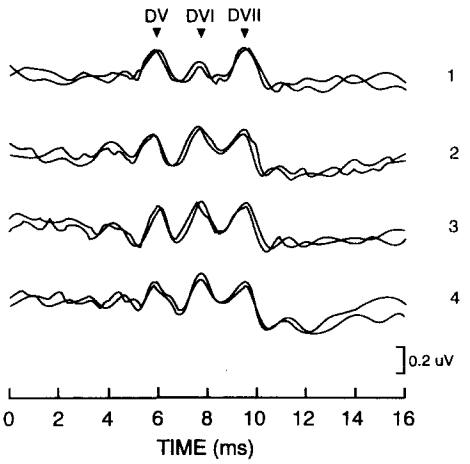


Fig. 5. Four duplicate BI traces showing intra-individual variation of the BI, recorded serially from the first subject in Fig. 3 during 5 months with an interval of about every 1.5 months. The clicks are fixed at 70 dB nHL and 10/s. Both latency and amplitude of wave DVII vary little.

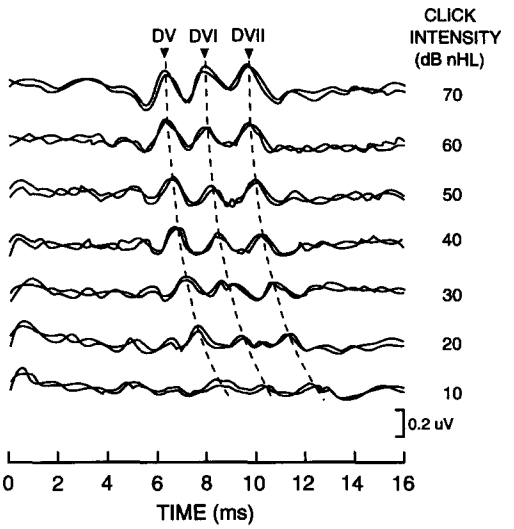


Fig. 6. Typical BI waveforms at different click intensity levels. The click rate is fixed at 10/s. BI wave latencies shift more at lower intensities than at higher intensities, while the interpeak intervals, especially DV–DVII, are essentially constant. BI wave amplitudes generally decrease with decreasing intensity.

ious click intensities. For the purpose of comparison between BI and BAEP latency-intensity functions, mean latencies of BAEP waves V, VI and VII in the summed monaural potentials are also plotted in Fig. 7. Wave latencies increased as a function of decreasing click intensity. These latency-intensity functions were slightly steeper at lower click intensities than at higher intensities. All wave latencies shifted by roughly the same amount, so that the latency-intensity function curves for these BI components

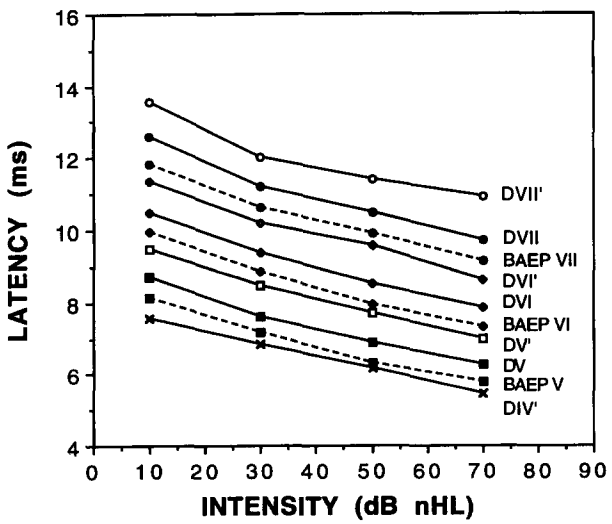


Fig. 7. Latency-intensity functions for various BI components at the clicks of 70, 50, 30 and 10 dB nHL. The clicks rate is 10/s. All BI wave latencies vary as a function of click intensity. The latency changes of BI components are more significant at lower intensities than at higher intensities, which are associated or concomitant with those of the corresponding BAEP waves in summed monaural potentials. All these BI and BAEP latency-intensity function curves are essentially parallel to each other.

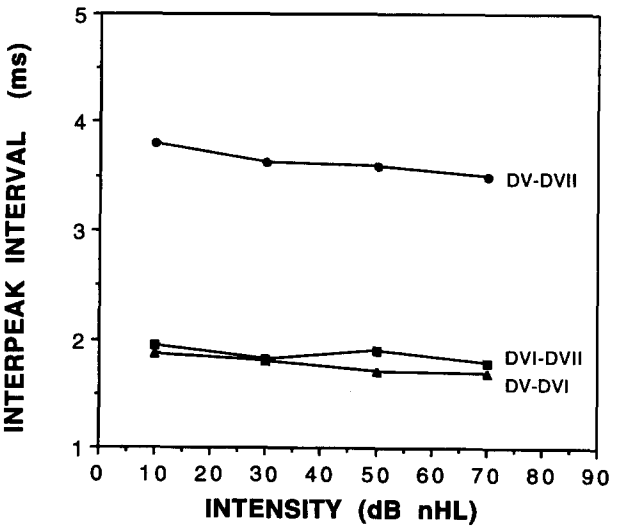


Fig. 8. Mean interpeak intervals of BI components at the click intensity levels of 70, 50, 30 and 10 dB nHL. The repetition rate of the clicks is 10/s. All intervals change very little at different intensities although DV–DVII interval tends to increase slightly with decreasing intensity.

were roughly parallel to each other. These changes were associated or concomitant with those of the corresponding BAEP waves (Fig. 7). Regression analysis showed that the latency shifted in 0.035, 0.040, 0.042, 0.044, 0.044, 0.047 and 0.044 ms/dB for the 7 BI components from wave DIV′ to wave DVII′ in sequence, respectively. These results suggest that the slopes of the functions tended to be slightly steeper for the later BI components than for the earlier components. All interpeak intervals did not demonstrate any significant changes with varying click intensity,

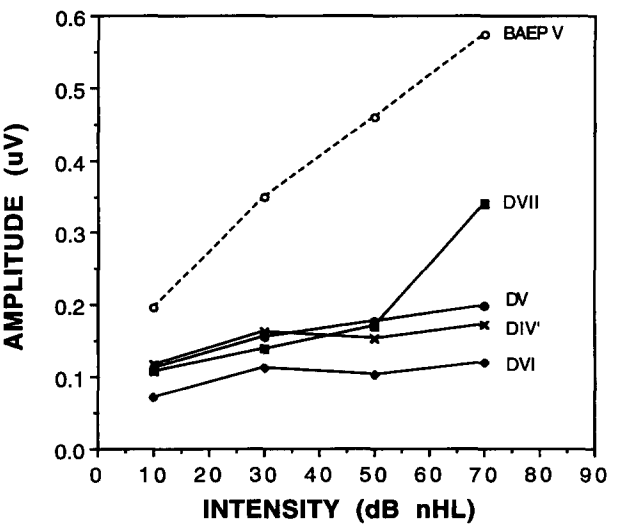


Fig. 9. Mean amplitudes of BI components at the click intensity levels of 70, 50, 30 and 10 dB nHL. The click rate is 10/s. Of the BI components, wave DVII has the largest amplitude at high intensity (70 dB nHL); it decreases markedly as the intensity decreases from high intensity to moderate intensity (50 dB nHL) and then decreases slightly with the intensity decreasing further. Note that the slope of the amplitude-intensity function for wave DV is much shallower compared to that for BAEP wave V.

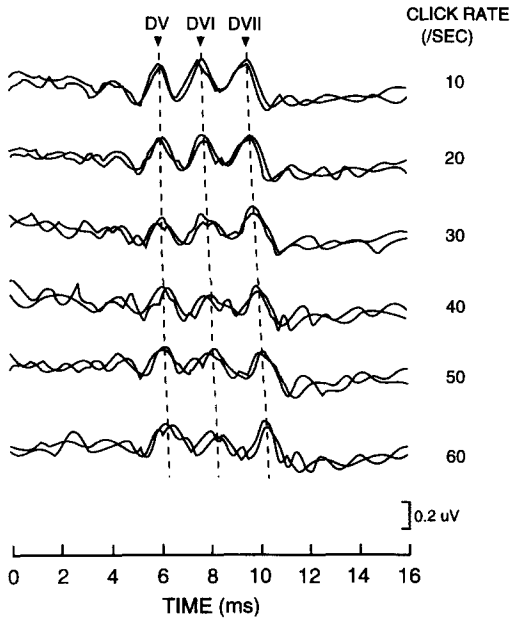


Fig. 10. Typical BI waveforms at different click repetition rates, recorded from the same subject in Fig. 5 in the third session. The click intensity is 70 dB nHL. BI waveform deteriorates at high click rates, although most BI components remain identifiable. Wave DVII is the most prominent BI component at all click rates.

although they tended to increase slightly at lower intensity levels (Fig. 8).

Fig. 9 presents the mean values of the amplitudes of the 4 major BI components, i.e. waves DIV′, DV, DVI and DVII, at various click intensities. Wave DV amplitude usually had the best linear relationship with the change in the intensity, whereas the amplitudes of waves DIV′ and DVI were more variable. Wave DVII usually decreased markedly when the click intensity decreased from 70 to 50 dB nHL and continued to decrease slightly with the intensity decreasing further. In Fig. 9, means of BAEP wave V amplitude (monaurally recorded from the left ear) are also plotted for the purpose of comparison between the changes in DV and the corresponding BAEP wave V with changing stimulus intensity. The amplitude of BAEP wave V decreased significantly with decreasing click intensity, while the change in wave DV of the BI was much less significant, as shown by the much shallower slope of amplitude-intensity function for wave DV compared to that of wave V. Regression analysis of the amplitudes of waves V and DV against click intensity were as follows: $y = 0.0776 + 0.0040x$ ($r = 0.88$, $P < 0.01$) for wave V, $y = 0.1022 + 0.0015x$ ($r = 0.84$, $P < 0.01$) for DV, where $y$ represents wave amplitude in $\mu$V and $x$ represents click intensity in dB nHL. Statistical comparison revealed that the two regression coefficients differed significantly ($t = 3.34$, $P < 0.01$).

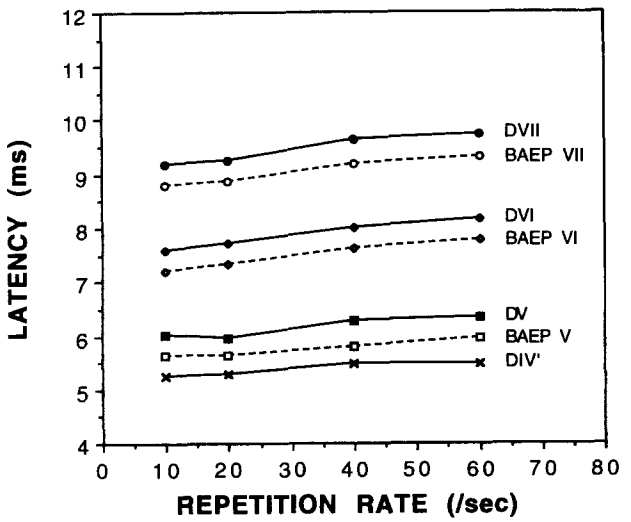


Fig. 11. Mean latencies of the 4 major BI components, i.e. waves DIV′, DV, DVI and DVII, at the click rates of 10, 20, 40 and 60/s. Mean latencies of BAEP waves V, VI and VII in the summed monaural potentials (L + R) are also plotted for the purpose of comparison. The click intensity is 70 dB nHL. As repetition rate increases, all BI and BAEP wave latencies increase slightly, with the later components changing slightly more than the earlier ones.

### 3.4. Effects of stimulus repetition rate on BI components

In general, better differentiated BI components could be derived when recorded at lower click repetition rates compared to those at higher rates. The 7 BI components were usually distinct at the rate of 10/s. Wave amplitudes decreased slightly at higher click rates. When the clicks were increased to above 20/s, BI waveform tended to be deteriorated and, sometimes, waves DV′, DVI, DVI′ and DVII′ were poorly differentiated (Fig. 10). At high click intensity levels, wave DVII usually was the most prominent BI component at all click rates used in this study. Most BI components could be reliably identified at all

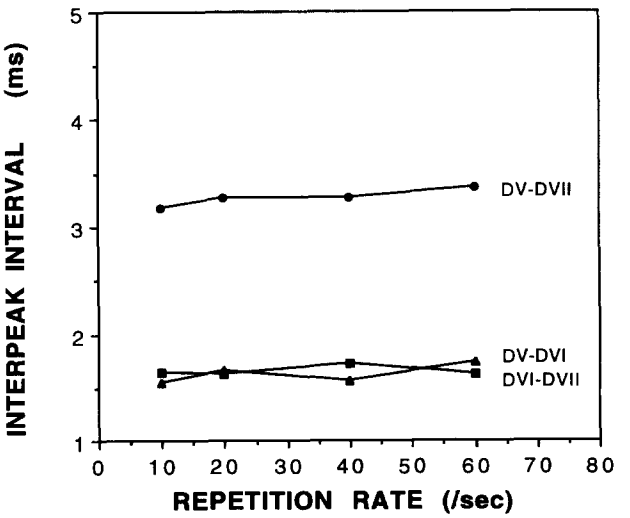


Fig. 12. Mean interpeak intervals of DV–DVII, DV–DVI and DVI–DVII at the click rates of 10, 20, 40 and 60/s. The click intensity is 70 dB nHL. DV–DVII interval shows a slight increase with increasing repetition rate.

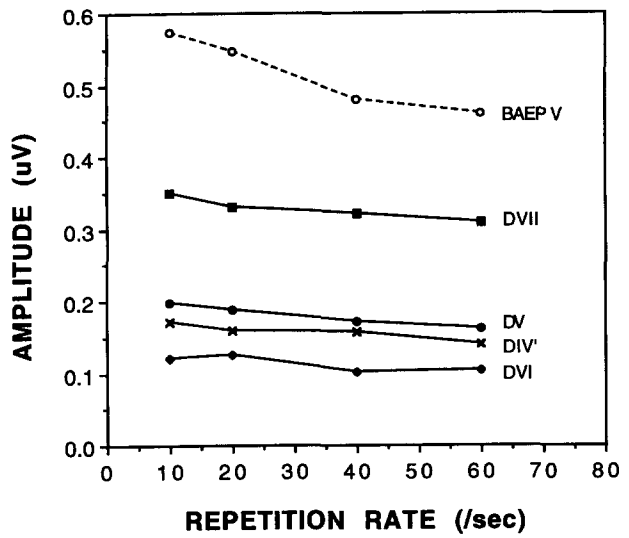


Fig. 13. Mean amplitudes of the 4 major BI components and BAEP wave V at different click rates. The click intensity is fixed at 70 dB nHL. All amplitudes tend to decrease slightly with increasing repetition rate.

repetition rates. At high click rates, the latencies of waves DIV′, DV, DVI and DVII and 3 interpeak intervals remained measurable with relatively accuracy, but wave amplitudes were difficult to determine accurately.

Figs. 11 and 12 present the means of wave DIV′, DV, DVI and DVII latencies and those of DV–DVI, DVI–DVII and DV–DVII intervals, respectively, recorded at the click rates of 10, 20, 40 and 60/s. Mean latencies of BAEP waves V, VI and VII in the summed monaural potentials are also plotted in Fig. 11 to show the comparison between BI and BAEP latency-rate functions. All BI and BAEP wave latencies increased slightly at the higher repetition rates, with the later components shifting more than the earlier components. The slopes of the latency-rate functions for various BI components were similar to those for the corresponding BAEP waves (Fig. 11). No statistically significant differences were found between the slopes for DV (0.073 ms/decade) and BAEP wave V (0.067 ms/decade), for DVI (0.114 ms/decade) and BAEP wave VI (0.118 ms/decade), and for DVII (0.119 ms/decade) and BAEP wave VII (0.107 ms/decade) (all $P > 0.05$). At higher repetition rates of stimulation, DV–DVII interval showed a tendency to increase slightly, while the two short intervals, i. e. intervals of DV–DVI and DVI–DVII, demonstrated no systematic and significant changes. As in the BAEP (monaurally recorded from the left ear), the amplitudes of all components in the BI tended to decrease slightly at higher click rates (Fig. 13). Occasionally, some BI amplitudes increased slightly at a higher click rate than at a lower rate.

The rate effect was also examined at the click intensity levels of 50 and 30 dB nHL in 4 subjects. Changes in the BI wave latencies, interpeak intervals and amplitudes were fundamentally similar to those recorded at 70 dB nHL.

## 4. Discussion

### *4.1. BI components in the BAEP and their origins*

Binaurally influenced neurons generally receive a predominantly excitatory input from on ear and either an excitatory or an inhibitory input from the other ear. In the lateral superior olivary nucleus, the inhibitory input is contralateral and the excitatory input is ipsilateral. Elsewhere within the auditory system the contralateral ear provides the excitatory input, due to a functional crossover in the brain-stem, with the ipsilateral ear providing either an excitatory or an inhibitory input. Binaural stimulation involves the delivery of separate and different acoustic signals to the two ears (dichotic stimulation) and produces a variety of response types which are often poorly predicted by the monotic responses. The present study showed that the 7 BI components coincide with the time domain of BAEP wave IV to wave VII. This finding provides further evidence to confirm that binaural processes at the level of the brain-stem occur mainly at higher levels of the brain-stem auditory pathway.

Binaural information is processed primarily in cells within the superior olivary complex, the first binaural station where afferent impulses from both ears connect for the first time, as well as at levels of the auditory pathway above the complex (Boudreau and Tsuchitani, 1968; Goldberg and Brown, 1969; Guinan et al., 1972; Moore, 1991). The superior olivary complex plays a crucial role in the initialisation of binaural processing (Jones and Van der Poel, 1990; Levine and Davis, 1991). The present study shows that reliable BI components in the BAEP occur in the region of waves IV and VII. The first reliable BI component in man is DIV′. The neural generator of wave IV is third-order neurons, located in the superior olivary complex and the lateral lemniscus. In intra-ponto-mesencephalic recording of BI in a human patient, Curio and Weigel (1990) observed that the first intrapontine BI component in man began as early as the peak of scalp-recorded wave III (mainly contributed by ipsilateral cochlear nucleus) and reached maximum between waves III and IV, or the downslope of wave III (probably generated by cochlear nucleus output fibres crossing the midline in the trapezoid body). The amplitude of the multiphasic BI waveform fell off with distance towards more rostral, mesencephalic recording sites, possibly due to the generator geometry. Previous studies on BI derived from scalp-recorded BAEP in humans often fail to find consistent and reliable BI component in this range. In the present study, we observed one or two small, less reliable additional BI components, which appeared before the onset of wave DIV′ and with a latency between BAEP waves III and IV, in some recordings. This observation suggests that binaural processing that occurs before wave DIV′ could be demonstrated in scalp-recorded BAEP, but compared to those at higher levels of the brain-stem auditory pathway, their detectabil-

ity in scalp recording is much lower. This may be due to an insufficient signal-to-noise ratio (Curio and Weigel, 1990).

The exact neural generators of these BI components in man remain to be determined. It has been recognized that the neural generators of later BAEP waves are complex in that more than one anatomical structure contributes to each wave and that each anatomical structure contributes to more than one wave. We observed that wave DV was the most stable BI component at all stimulus conditions. This is in accordance with previous reports that the major BI component occurs at the downslope of BAEP wave V (Hosford et al., 1979; Ainslie and Boston, 1980; Dobie and Norton, 1980; Hosford-Dunn et al., 1981; Levine, 1981; Wrege and Starr, 1981; Kelly-Ballweber and Dobie, 1984; Ito et al., 1988; McPherson et al., 1989; Levine and Davis, 1991). It appears that the generators of BAEP wave V play a major role for binaural processing of inputs from both ears. The exact generators of wave V are still a controversial issue. For more than two decades, this wave has been postulated by many authors to originate from the inferior colliculus, the largest nuclear structure in the human brainstem auditory pathway (e.g. Jewett and Romano, 1972; Funai and Funasaka, 1983; Moore, 1987). However, increasing evidence suggests that wave V is more likely to originate in the lateral lemniscus (Møller and Jannetta, 1982a; Møller and Jannetta, 1982b; Fullerton and Kiang, 1990) and less likely in the inferior colliculus. In the cat, neurons in the lateral superior olive and the medial nucleus of the trapezoid body seem to have a major role in generating waves IV and V (Zaaroor and Starr, 1991a; Zaaroor and Starr, 1991b). Some recent human data suggests that wave V may originate at or rostral to the inferior colliculus (Durrant et al., 1994). Levine and Davis (1991) reported that in the presence of high passed masking noise (4000 Hz cut-off), little activity occurs at the time the click-evoked $\beta$, corresponding to DV in the present study, would be expected. They concluded that $\beta$ is principally due to the high-frequency components of the broad band click so that it is through the activity in high characteristic frequency auditory nerve fibers that click-evoked $\beta$ is generated, and $\beta$ is possibly generated by the high-frequency cells of the medial superior olive, the major nucleus of the human superior olivary complex.

Waves VI and VII in the BAEP are presumably produced by a lateral firing population of neurons and axons in the inferior colliculus and its brachium or the first evoked activity in the nuclei of medial geniculate (Hashimoto et al., 1981; Møller and Jannetta, 1983; Moore, 1987) or thalamocortical radiations (Legatt et al., 1986). The presence of waves DVI, which probably corresponds to peak $\delta$ in Levine's study (Levine, 1981), and DVII in the BI waveform suggests that there may be neuronal interaction for binaural processing in the regions rostral to the generators of BAEP wave V.

The latencies and interpeak intervals of BI components are fairly constant both across subjects and within subjects, while wave amplitudes are relatively variable, which is similar to our findings in the BAEP (Jiang et al., 1991c; Jiang et al., 1993).

### 4.2. Wave DVII: a possible neurogenic BI component

It is known that BI waveform may include intrinsic and extraneous neural elements. Although wave DVII exists consistently at various stimulus conditions, it is essential to exclude the effects of extraneous factors such as middle ear reflex (MER) and acoustic cross-talk (ACT).

Since the contractions of middle ear muscles reduce sound transmission through the middle ear and are greater for binaural than monaural stimulation, each cochlea may receive sounds that are at a lower intensity during binaural stimulation than during monaural stimulation (Møller, 1962). This difference in intensity between binaural and monaural stimulation could produce a difference between the binaural evoked potentials and the summed monaural evoked potentials. Yet, the effect of the MER on BI can be negligible (Levine, 1981). There are several reasons for this. The stimulus intensity at the cochlea is probably at most 5 dB lower for binaural than for monaural stimulation (Møller, 1962). The latencies of BAEP waves should be longer for the binaural than for the monaural evoked potentials if the MER attenuates the sounds more for binaural than for monaural stimulation, because the latencies of BAEP waves increase at lower stimulus intensity. In fact, the latencies of BAEP waves are slightly shorter in the binaural evoked potentials than in the monaural ones. The MER attenuates predominantly low-frequency components of sound. Moreover, since this attenuation occurs before the sounds reach the cochlea, a similar effect might be expected upon the entire BAEP or all BAEP waves. The amplitudes of earlier BAEP waves are more sensitive to sound intensity than the later ones, and thus the fact that earlier BAEP waves do no show reproducible and consistent BI further rules out any significant MER contribution to BI. At high repetition rate of stimulation, however, the MER could have some influence on the recorded potentials.

It has been reported that ACT may have a significant effect upon BI waveform at high stimulus intensities (Ainslie and Boston, 1980; Levine, 1981). During high-intensity monaural stimulation, the ipsilateral ear responds to the direct, high-intensity stimuli, producing shorter latency potentials, while the contralateral ear to the crossed, low-intensity stimuli transmitted across the skull produces longer latency potentials. Consequently, the BAEP may include the potentials of the contralateral ear to the ACT as well as those of the ipsilateral ear to the direct stimuli. On the contrary, during binaural stimulus condition, BAEP only contains the potentials of the ipsilateral ear to the direct stimuli, since the crossed stimuli are probably masked by the direct stimuli to the ear and neither ear responds to the delayed and attenuated ACT. As a result,

a BI component produced by ACT rather than by neural interaction will be present in the BI waveform derived from subtracting binaural BAEP trace from summed monaural BAEP traces or vice versa at high-intensity stimulation. It is therefore important to rule out the effect of ACT on BI components in the study of BI. The ACT effect can be reduced or avoided at moderate and low intensity levels, because ACT occurs mainly at high stimulus intensities (Ainslie and Boston, 1980; Levine, 1981). At moderate and low stimulus intensities, bone-conducted ACT may not contribute to the BI (Dobie and Berlin, 1979; Hosford et al., 1979; Dobie and Norton, 1980; Levine, 1981). Levine (1981) reported that the maximum level to avoid ACT is 46 dB above the threshold of the opposite ear. Since BAEP usually cannot be detected until it is at least 5 dB above threshold, a level of around 51 dB may be still safe. The present study found that wave DVII decreased markedly with decreasing stimulus intensity from 70 to 50 dB nHL. Nevertheless, this BI component remained clearly identifiable at the clicks of 50 HL and less, the intensity levels below any possibility of ACT. These observations suggest that wave DVII is due to intrinsic binaural neuronal interaction, although ACT may account for a part of this component at high stimulus intensity levels. It thus appears that there are potentials that are generated by binaurally influenced neurons in the brain-stem structures rostral to the generators of BAEP wave V.

Since the head size in infants is much smaller than that in adults, the ACT effect ought to be more significant in infants than in adults. Any contributions to the BI waveform by the ACT effect should be more significant in infants, and thus wave DVII would be relatively more prominent if this component is produced primarily by the ACT effect. In fact, we found that wave DVII was much less prominent in term neonates relative to that in the adults, even at the high-intensity stimulation (Jiang and Tierney, 1996b). This component was difficult to identify in preterm infants up to around 35 weeks of gestation (Jiang et al., 1996). These observations provide further evidence that wave DVII is neural in origin.

### *4.3. Changes in BI components with stimulus intensity*

Our previous studies have shown that all BAEP wave latencies shift with changing stimulus intensity by roughly the same amount so that the latency-intensity functions for various BAEP components almost parallel each other and the interpeak intervals change little at various intensity levels (Liu and Jiang, 1991). It appears that the changes in BAEP wave latencies with stimulus intensity are transferred originally from the intensity-dependent change in wave I latency. In other words, intensity effect on the BAEP occurs primarily in the peripheral auditory system. This function may be altered in some peripheral hearing disorders such as sensorineural hearing loss (Jiang, 1995). The present study showed that the latencies of BI components varied as a function of stimulus intensity while the interpeak intervals were affected little or very slightly by changing intensity levels. These observations were fundamentally the same as those of BAEP components in the monaurally and binaurally recorded potentials. Therefore, the intensity effect on BI components is supposed to occur prior to wave DV and, based on our previous findings of the intensity effect on BAEP components (Jiang et al., 1991c; Liu and Jiang, 1991), is most likely to be peripheral in origin.

In this study the latencies of later BI components tend to shift with stimulus intensity slightly more than those of the earlier components and the interpeak intervals tend to increase slightly at lower intensities. These observations may be produced by slight alteration in waveforms of the BI components, especially the later components, at different stimulus intensity levels.

The amplitude of BAEP wave V has been shown to be a useful variable in certain clinical conditions (Jiang et al., 1993; Jiang and Tierney, 1996a). We have previously observed that the amplitude of BAEP wave V changes linearly with varying stimulus intensity (Jiang, 1991). The present study shows that the amplitude of BI wave DV also varies linearly with stimulus intensity, but this change is less remarkable. The amplitude of wave DV has been reported to approach about 16–25% of the expected amplitude of wave V in the summed monaural potentials (e.g. Levine, 1981; McPherson et al., 1989). In this study, wave DV was found to account for 24% of the magnitude of BAEP wave V in the summed monaural potentials. This percentage increased slightly at lower stimulus intensity levels, suggesting that the decrease in wave DV is less significant compared to that in BAEP wave V.

### *4.4. Changes in BI components with repetition rate*

Studies on stimulus rate effect have generally found that BAEP wave latencies increase and amplitudes decrease with increasing stimulus repetition rate (Pratt and Sohmer, 1976; Don et al., 1977; Scott and Harkins, 1978; Pratt et al., 1981; Gerling and Finitzo-Hieber, 1983; Jiang et al., 1991a; Jiang et al., 1991b). The present study shows that the BI components are also affected by varying stimulus repetition rate. Increasing stimulus rate increases BI wave latencies and interpeak intervals and decreases wave amplitudes slightly. These observations are generally similar to those we observed in BAEP waves and are associated or concomitant with those of the corresponding BAEP waves in monaurally and binaurally recorded potentials.

Variation in BAEP measures with changing stimulus rate may reflect changes in central synaptic efficacy (Pratt and Sohmer, 1976; Don et al., 1977; Gerling and Finitzo-Hieber, 1983) or metabolic changes at the receptor

level or changes in neural activity within the brain-stem (Thornton and Coleman, 1975; Don et al., 1977). The decrease in amplitude and the variation of morphology at high stimulus rates may be caused by reduced synapse synchronisation, or temporal dispersion of the afferent volleys, as well as changes in the number of primary afferent fibres activated (Scott and Harkins, 1978). The slight decrease in wave amplitudes of the BI, derived from the higher order brain-stem nuclei, suggests that at high repetition rate the number of active fibres reaching the next nucleus may still have been sufficient to cause near maximal excitation. At higher repetition rates, the latencies of later BI components increase slightly more than those of earlier components, producing a slight increase in interpeak intervals. This indicates that increasing stimulus rate has a greater effect on the latency for the later BI components as compared to the earlier ones, which is similar to our previous observations on the BAEP wave latencies (Jiang et al., 1991b). This may be primarily attributed to an accumulation of the rate effect on the series of earlier components, since the more synapses which exist between the first-order neurons and progressively more rostral generators, the more aggregate synaptic fatigue could occur.

The present study demonstrates that BI waveform is better differentiated at lower stimulus repetition rates than at higher rates. We suggest that low repetition rates, e.g. 10/s, are preferred for routine derivation of BI, so that both latency and amplitude could be determined more precisely. Some of the previous studies have shown that abnormal rate effects in the BAEP are associated with pathology in the central nervous system (e.g. Pratt et al., 1981). Whether increasing stimulus rate could be used in deriving BI for testing the dynamic properties of the brainstem auditory systems is not known and remains an interesting issue to be investigated.

### *4.5. Nomenclature of BI components*

So far, there has been no uniform nomenclature for BI components. The nomenclature used by the previous authors is largely arbitrary. Since there are two contrary ways to derive BI waveform, it would be inappropriate to define the BI deflection as positive or negative. In this study we noted that each BI component occurs closely in association or concomitance with each corresponding BAEP wave and this is independent of varying stimulus intensity and repetition rate. We therefore designated BI components, based on their latency range, in association with the corresponding BAEP waves.

In conclusion, the present study shows that the BI components in the BAEP occur between the latency range of 5 and 11 ms and coincide consistently with the latency range of BAEP waves IV through VII. Waves DIV′, DV, DVI and DVII are the four major and reliable BI components. Wave DVII, which has never been described before, may be neural in origin. Three interpeak intervals of the BI, i.e. DV–DVII, DV–DVI and DVI–DVII, are essentially constant. The changes in BI components with stimulus intensity and repetition rate are associated or concomitant with those of the corresponding BAEP components in monaural and binaural potentials.

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